

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claims 1-28 (Cancelled).

29. (New) A method for the diagnosis of a disease selected from the group consisting of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and gestational diabetes, comprising determining the expression level of a peptide or polypeptide with a sequence selected from the group consisting of:

- a) an amino acid sequence as presented in SEQ ID NO: 2 or 4;
- b) an amino acid sequence exhibiting a sequence identity with any of the amino acid sequences according to a) of at least 85% over 100 amino acid residues; and
- c) a fragment of any of the sequences defined above which is at least 5 amino acids in length.

30. (New) The method according to claim 29, wherein the sequence is that shown in SEQ ID NO: 8.

31. (New) The method of claim 29, wherein the expression level, ligand, or nucleic acid is used in conjunction with:

(1) a means or a diagnostic agent for the measurement of expression of any of the genes or proteins selected from the group consisting of

- a) EPAS-1/HIF-2 α ;
- b) neurokinin B;
- c) TIMP-1;
- d) VEGFR-1;
- e) VEGF;
- f) IGFBP-1;
- g) IGFBP-3;
- h) matrix metalloproteinase-2;
- i) leptin;

- j) PAI-1;
 - k) IGF-1;
 - l) angiopoietin-2;
 - m) decorin;
 - n) PlGF;
 - o) HLA-G;
 - p) HB-EGF;
 - q) TGF- β 3;
 - r) MIFR-2;
 - s) LIM; and
 - t) EBI3;
- (2) diagnostic tools for the measurement of blood pressure or protein content of the urine, or
- (3) a combination of (1) and (2).

32. (New) A method for the diagnosis of a disease selected from the group consisting of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and gestational diabetes, comprising measuring the amount of a ligand bound to a peptide or polypeptide, wherein the ligand specifically binds to the peptide or polypeptide, and the peptide or polypeptide has a sequence selected from the group consisting of

- a) an amino acid sequence as presented in SEQ ID NO: 2 or 4;
- b) an amino acid sequence exhibiting a sequence identity with any of the amino acid sequences according to a) of at least 85% over 100 amino acid residues; and
- c) a fragment of any of the sequences defined above which is at least 5 amino acids in length.

33. (New) The method according to claim 32, wherein the ligand is used for measurement of the expression level of the peptide or polypeptide.

34. (New) The method according to claim 32, wherein the sequence is as shown in SEQ ID NO: 8.

35. (New) The method according to claim 32, wherein the ligand is selected from the group consisting of:

- a) KB-R7785 or a derivative thereof;
- b) TIMP-1, TIMP-2, TIMP-3, IGFBP-5, PKC- δ , α -actinin, α -actinin-2, src, Grb-2, or syndecan-4;
- c) antibodies;
- d) nucleic acid or protein aptamers; and
- e) fragments or derivatives of any of the substances defined in b), c), or d).

36. (New) The method of claim 32, wherein the expression level, ligand, or nucleic acid is used in conjunction with:

- (1) diagnostic tools for the measurement of blood pressure or protein content of the urine;
- (2) a means or a diagnostic agent for the measurement of expression of any of the genes or proteins selected from the group consisting of:
 - a) EPAS-1/HIF-2 α ;
 - b) neurokinin B;
 - c) TIMP-1;
 - d) VEGFR-1;
 - e) VEGF;
 - f) IGFBP-1;
 - g) IGFBP-3;
 - h) matrix metalloproteinase-2;
 - i) leptin;
 - j) PAI-1;
 - k) IGF-1;
 - l) angiopoietin-2;
 - m) decorin;
 - n) PlGF;
 - o) HLA-G;
 - p) HB-EGF;
 - q) TGF- β 3;
 - r) MIFR-2;
 - s) LIM; and
 - t) EBI3; or
- (3) a combination of (1) and (2).

37. (New) The method of claim 32, wherein the nucleic acid, ligand or, additionally, diagnostic agent is present on an array.

38. (New) A method for the diagnosis of a disease selected from the group consisting of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and gestational diabetes, comprising determining the expression level of a nucleic acid molecule comprising a nucleic acid selected from the group consisting of

- a) a nucleic acid with a sequence as presented in SEQ ID NO: 1 or 3;
- b) a nucleic acid with a sequence that exhibits a sequence identity with any of the sequences defined in a) of at least 70% over 300 residues;
- c) a nucleic acid which is capable of hybridizing with the nucleic acid as defined in a), or b) under conditions of medium or high stringency;
- d) a nucleic acid with the antisense-sequence of any of the sequences defined in a), b) or c);
- e) a fragment of any of the nucleic acids as defined in a), b), c), or d), wherein the fragment is at least 15 nucleotides in length; and
- f) an RNA corresponding to any of the sequences defined in a), b), c), d) or e).

39. (New) The method of claim 38, wherein the fragment has a sequence consisting of SEQ ID NO: 7, 13, 14, 15, 16, 5, 10, 11, or 12, or wherein the fragment has the sequence of a fragment thereof with at least 15 nucleotides in length.

40. (New) A method for the diagnosis of a disease selected from the group consisting of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and gestational diabetes, comprising determining a nucleic acid molecule comprising a nucleic acid selected from the group consisting of

- a) a nucleic acid with a sequence as presented in SEQ ID NO: 1 or 3;
- b) a nucleic acid with a sequence that exhibits a sequence identity with any of the sequences defined in a) of at least 70% over 300 residues;
- c) a nucleic acid which is capable of hybridizing with the nucleic acid as defined in a), or b) under conditions of medium or high stringency;
- d) a nucleic acid with the antisense-sequence of any of the sequences defined in a), b) or c);
- e) a fragment of any of the nucleic acids as defined in a), b), c), or d), wherein the fragment is at least 15 nucleotides in length; and

f) an RNA corresponding to any of the sequences defined in a), b), c), d) or e);

41. (New) The method according to claim 40, wherein the fragment has a sequence consisting of SEQ ID NO: 7, 13, 14, 15, 16, 5, 10, 11, or 12, or wherein the fragment has the sequence of a fragment thereof with at least 15 nucleotides in length.

42. (New) The method of claim 37, wherein the expression level, ligand, or nucleic acid is used in conjunction with:

(1) diagnostic tools for the measurement of blood pressure or protein content of the urine;

(2) a means or a diagnostic agent for the measurement of expression of any of the genes or proteins selected from the group consisting of

- a) EPAS-1/HIF-2 α ;
- b) neurokinin B;
- c) TIMP-1;
- d) VEGFR-1;
- e) VEGF;
- f) IGFBP-1;
- g) IGFBP-3;
- h) matrix metalloproteinase-2;
- i) leptin;
- j) PAI-1;
- k) IGF-1;
- l) angiopoietin-2;
- m) decorin;
- n) PlGF;
- o) HLA-G;
- p) HB-EGF;
- q) TGF- β 3;
- r) MIFR-2;
- s) LIM; and
- t) EBI3; or

(3) a combination of (1) and (2).

43. (New) The method of claim 40, wherein the nucleic acid, ligand or, additionally, diagnostic agent is present on an array.

44. (New) A method for the identification of ligands binding specifically to a peptide or polypeptide or encoded by a nucleic acid molecule, comprising the following steps:

- a) contacting the polypeptide with at least one candidate for a ligand;
 - b) measuring the binding of the candidate for a ligand to the polypeptide,
- wherein:

(1) the peptide or polypeptide has a sequence selected from the group consisting of:

- a) an amino acid sequence as presented in SEQ ID NO: 2 or 4;
 - b) an amino acid sequence exhibiting a sequence identity with any of the amino acid sequences according to (1a) of at least 85% over 100 amino acid residues;
- and
- c) a fragment of any of the amino acid sequences defined above which is at least 5 amino acids in length; and

(2) the nucleic acid molecule comprises a nucleic acid selected from the group consisting of:

- a) a nucleic acid with a sequence as presented in SEQ ID NO: 1 or 3;
- b) a nucleic acid with a sequence that exhibits a sequence identity with any of the sequences defined in (2a) of at least 70% over 300 residues;
- c) a nucleic acid which is capable of hybridizing with the nucleic acid as defined in (2a), or (2b) under conditions of medium or high stringency;
- d) a nucleic acid with the antisense-sequence of any of the sequences defined in (2a), (2b) or (2c);
- e) a fragment of any of the nucleic acids as defined in (2a), (2b), (2c), or (2d), wherein the fragment is at least 15 nucleotides in length; and
- f) an RNA corresponding to any of the sequences defined in (2a), (2b), (2c), (2d) or (2e).

45. (New) A method for the diagnosis of a disease selected from preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and gestational diabetes comprising the following steps:

- a) bringing a biopsy or bodily fluid sample into contact with a nucleic acid or a specifically binding ligand, and
 - b) detecting the binding of the nucleic acid or ligand;
- wherein:

(1) the specifically binding ligand specifically binds to a peptide or polypeptide having a sequence selected from the group consisting of:

- a) an amino acid sequence as presented in SEQ ID NO: 2 or 4;
- b) an amino acid sequence exhibiting a sequence identity with any of the amino acid sequences according to (1a) of at least 85% over 100 amino acid residues; and
- c) a fragment of any of the sequences defined above which is at least 5 amino acids in length; and

(2) the nucleic acid molecule comprises a nucleic acid selected from the group consisting of:

- a) a nucleic acid with a sequence as presented in SEQ ID NO: 1 or 3;
- b) a nucleic acid with a sequence that exhibits a sequence identity with any of the sequences defined in (2a) of at least 70% over 300 residues;
- c) a nucleic acid which is capable of hybridizing with the nucleic acid as defined in (2a), or (2b) under conditions of medium or high stringency;
- d) a nucleic acid with the antisense-sequence of any of the sequences defined in (2a), (2b) or (2c);
- e) a fragment of any of the nucleic acids as defined in (2a), (2b), (2c), or (2d), wherein the fragment is at least 15 nucleotides in length; and
- f) an RNA corresponding to any of the sequences defined in (2a), (2b), (2c), (2d) or (2e).

46. (New) A diagnostic composition comprising:

(1) a specifically binding ligand that specifically binds to a peptide or polypeptide having a sequence selected from the group consisting of:

- a) an amino acid sequence as presented in SEQ ID NO: 2 or 4;
- b) an amino acid sequence exhibiting a sequence identity with any of the amino acid sequences according to (1a) of at least 85% over 100 amino acid residues; and
- c) a fragment of any of the sequences defined above which is at least 5 amino acids in length; or

(2) a nucleic acid molecule selected from the group consisting of:

- a) a nucleic acid with a sequence as presented in SEQ ID NO: 1 or 3;
- b) a nucleic acid with a sequence that exhibits a sequence identity with any of the sequences defined in (2a) of at least 70% over 300 residues;

- c) a nucleic acid which is capable of hybridizing with the nucleic acid as defined in (2a), or (2b) under conditions of medium or high stringency;
- d) a nucleic acid with the antisense-sequence of any of the sequences defined in (2a), (2b) or (2c);
- e) a fragment of any of the nucleic acids as defined in (2a), (2b), (2c), or (2d), wherein the fragment is at least 15 nucleotides in length; and
- f) an RNA corresponding to any of the sequences defined in (2a), (2b), (2c), (2d) or (2e).

47. (New) The diagnostic composition of claim 46, further comprising:

(1) diagnostic tools for the measurement of blood pressure or protein content of the urine;

(2) a means or a diagnostic agent for the measurement of expression of any of the genes or proteins selected from the group consisting of

- a) EPAS-1/HIF-2 α ;
- b) neurokinin B;
- c) TIMP-1;
- d) VEGFR-1;
- e) VEGF;
- f) IGFBP-1;
- u) IGFBP-3;
- v) matrix metalloproteinase-2;
- w) leptin;
- x) PAI-1;
- y) IGF-1;
- z) angiopoietin-2;
- aa) decorin;
- bb) PlGF;
- cc) HLA-G;
- dd) HB-EGF;
- ee) TGF- β 3;
- ff) MIFR-2;
- gg) LIM; and
- hh) EBI3; or

(3) a combination of (1) and (2).

comprising a nucleic acid as defined in claim 38.

48. (New) The diagnostic composition of claim 46, wherein the nucleic acid or ligand is present on an array.

49. (New) The diagnostic composition of claim 47, wherein the diagnostic agent or tool is present on an array.

50. (New) A diagnostic kit comprising a nucleic acid or ligand as defined in claim 46.

51. (New) A diagnostic kit comprising a nucleic acid or ligand, and further comprising a diagnostic agent or tool, all as defined in claim 47.

52. (New) The diagnostic kit of claim 50, wherein the nucleic acid or ligand is present on an array.

53. (New) The diagnostic kit of claim 51, wherein the nucleic acid or ligand is present on an array, and the diagnostic agent or tool is also present on an array.

54. (New) A method for the treatment of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, or gestational diabetes, comprising administering to a patient in need thereof a therapeutically effective amount of a nucleic acid molecule comprising a nucleic acid selected from the group consisting of:

- a) a nucleic acid with a sequence as presented in SEQ ID NO: 1 or 3;
- b) a fragment of any of the nucleic acids as defined in a), wherein the fragment is at least 15 nucleotides in length;
- c) a nucleic acid with the antisense sequence of any of the sequences defined in a), or b); and
- d) single-stranded or double-stranded RNA, preferably siRNA, with a sequence corresponding to any of the sequences defined in a), b), or c).

55. (New) The method according to claim 54, wherein the fragment consists of SEQ ID NO: 5 or 7 or of a fragment thereof wherein the fragment is at least of 15 nucleotides in length.

56. (New) The method according to claim 54, wherein the symptoms of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, or gestational diabetes, are selected from the group consisting of intravascular coagulation, blood platelet destruction, placental abruption, or high blood pressure are treated.

57. (New) A method for the treatment of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, or gestational diabetes, comprising administering to a patient in need thereof a therapeutically effective amount of an inhibitor of the biological activity of a peptide or polypeptide with a sequence selected from the group consisting of:

- a) an amino acid sequence as presented in SEQ ID No. 2 or 4;
- b) an amino acid sequence exhibiting a sequence identity with any of the sequences according to a) of at least 85% over 100 residues; and
- c) a fragment of any of the sequences as defined above wherein the fragment is at least of 5 amino acids in length.

58. (New) The method according to claim 57, wherein the fragment has a sequence consisting of SEQ ID NO: 8 or of a fragment thereof wherein the fragment is at least of 5 amino acids in length.

59. (New) The method according to claim 57, wherein the inhibitor is selected from the group consisting of a disintegrin domain metalloproteinase inhibitor, KB-R7785, a TIMP, TIMP-3 or a fragment thereof, α_2 -Macroglobulin, and an antibody directed against ADAM 12.

60. (New) The method according to claim 57, wherein additionally HB-EGF is administered.

61. (New) The method according to claim 57, wherein the symptoms of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, or gestational diabetes to be treated are selected from the group consisting of intravascular coagulation, blood platelet destruction, placental abruption, and high blood pressure.

62. (New) A method for identification of an inhibitor of the biological activity of a peptide or polypeptide, comprising the following steps:

- a) contacting said peptide or polypeptide with a suitable substrate, e.g. HB-EGF, and
- b) measuring the decrease in processing of the substrate in the presence as compared to the absence of a candidate for an inhibitor molecule;

wherein the peptide or polypeptide has a sequence selected from the group consisting of:

- 1) an amino acid sequence as presented in SEQ ID No. 2 or 4;
- 2) an amino acid sequence exhibiting a sequence identity with any of the sequences according to 1) of at least 85% over 100 residues; and
- 3) a fragment of any of the sequences as defined above wherein the fragment is at least of 5 amino acids in length.

63. (New) The method according to claim 62, wherein the candidate for an inhibitor is a substrate or a ligand of a peptide or polypeptide, wherein the peptide or polypeptide has a sequence selected from the group consisting of:

- 1) an amino acid sequence as presented in SEQ ID No. 2 or 4;
- 2) an amino acid sequence exhibiting a sequence identity with any of the sequences according to 1) of at least 85% over 100 residues; and
- 3) a fragment of any of the sequences as defined above wherein the fragment is at least of 5 amino acids in length.

64. (New) A method for the preparation of a pharmaceutical composition comprising:

(A) identifying an inhibitor of a nucleic acid, peptide, or polypeptide, wherein:

(1) the peptide or polypeptide has a sequence selected from the group consisting of:

- i) an amino acid sequence as presented in SEQ ID No. 2 or 4;
- ii) an amino acid sequence exhibiting a sequence identity with any of the sequences according to (A.1.i) of at least 85% over 100 residues; and
- iii) a fragment of any of the sequences as defined above wherein the fragment is at least of 5 amino acids in length; and

(2) the nucleic acid is selected from the group consisting of:

- i) a nucleic acid with a sequence as presented in SEQ ID NO: 1 or 3;
- ii) a fragment of any of the nucleic acids as defined in (A.2.i), wherein the fragment is at least 15 nucleotides in length;

- iii) a nucleic acid with the antisense sequence of any of the sequences defined in (A.2.i), or (A.2.ii);
 - iv) single-stranded or double-stranded RNA, preferably siRNA, with a sequence corresponding to any of the sequences defined in (A.2.i), (A.2.ii), or (A.2.iii);
- (B) wherein the nucleic acid, peptide or polypeptide is identified by contacting said nucleic acid, peptide or polypeptide with a suitable substrate, e.g. HB-EGF, followed by measuring the decrease in processing of the substrate in the presence as compared to the absence of a candidate for an inhibitor molecule;
- (C) synthesizing the nucleic acid, peptide, or polypeptide in suitable amounts; and
- (D) formulating the nucleic acid, peptide, or polypeptide into a pharmaceutical composition.